

Title: xxx

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Submitted: 01-04-2024

Accepted: 10-04-2024

ABSTRACT-

In Ancient times ,vitiligo disease spread all over the world more than 1500 years BC.Both pre hindu vedic and ancient egyptians give the record of vitiligo depigmented macules,and the vitiligo cause due to lack of melanin.

In ancient times,the hakims and vaidyas and vitiligo were treated with a mixture of(tar,honey,oil)in Egypt.

In India,vitiligo was treated with a combination of herbs and stimulated melanin production in the skin.

So,it was difficult to treat vitiligo then the hakims and vaidyas treated the vitiligo by the AYUSH System.

A-Ayurveda

S-Siddha

U-Unani

In Ayurveda treatment the bakuchi(p.corylifolia)seeds (churna powder is used in vitiligo)used topical and systemic application.

In siddha system of medicine, on the basis of three vital humors ,siddha system classifies vitiligo(venpadai)as- “Vatha Venpadai”

“Pitha Venpadai”

“Kaba venpadai”

In the Unani system, the knowledge of unani system medicine as a healing system was collected by “Hakim ibn sina”(known as Avicena) in 980 CE in Persia.

Unani system/medicine ,It helps to treat and induce repigmentation.

Skin cells(melanocytes)are responsible for producing melanin ,the substance that gives pigmentation to the skin.

In this review ,we provide an overview of the currently known herbal medicine/drug.

The herbal drug that inhibit the action of vitiligo and stimulate the melanin,and the synthetic medicine for vitiligo are derived from chemical synthesis,these are synthetically prepared medicine medicine are well designed , that drug inhibit the action of vitiligo .But it gives several adverse drug reaction .So,the review aims to a provide a comprehensive overview of the current state of knowledge about vitiligo.

KEYWORD- Therapy, vitiligo,herbal therapy, deficiency of melanin ,active API,analysis of herbal drug byHPLC and UV

HISTORY- Its first description dates back more than 3000 yrs.The vitiligo first discovered by the Roman physician celsus

- 1) The ebers papyrus in 1550 BC mentioned two forms of depigmentation that could be interpreted as leprosy and depigmentation resembling vitiligo.
- 2) In 1400BCwhite leprosy spots were called sveta khushtha in the atharva veda
- 3) In 1200 BC Japanese Shinto prayers described depigmentation in the Amarakosa.
- 4) Around 600BC, the ashtanga hridaya explained prognostic factor of depigmentation
- 5) In summary around 4000 yrs of known history elapsed from the time man became aware of disturbing white spots skin until the melanocytes was finally identified as the responsible actor for depigmentation and other pigmentary disorder
- 6) In 1879 moritz kaposi was one of the DOPA reactions demonstrating the melanin synthesizing enzyme tyrosinase within the melanocyte.

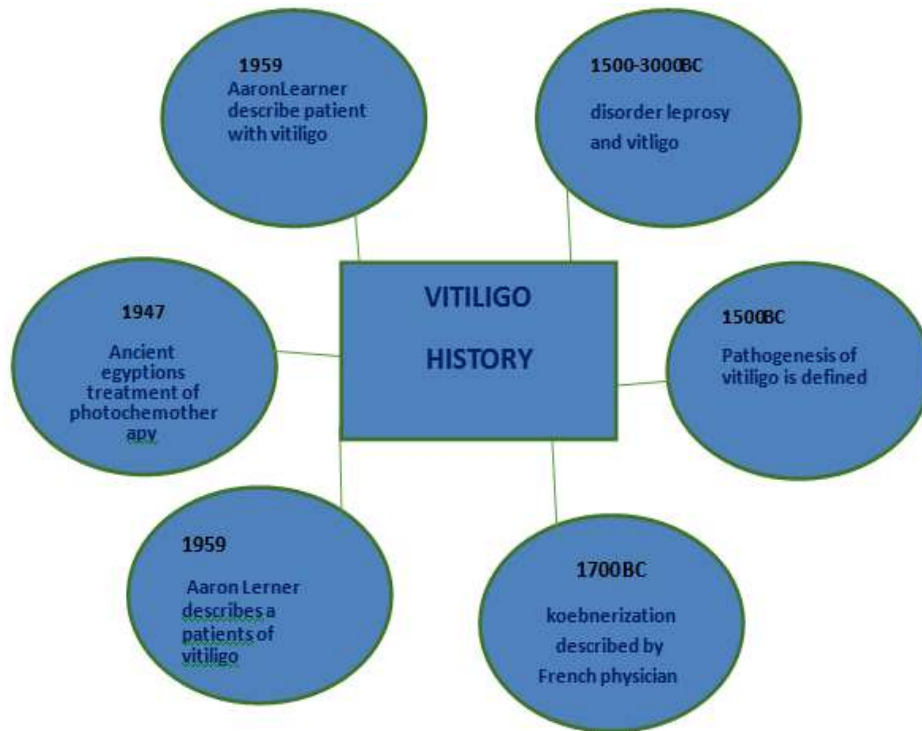


Chart No-1

I. INTRODUCTION-

Autoimmune Disorder-Vitiligo is an autoimmune disorder ,also a common pigmentary disorder of the skin.The vitiligo is neither life threatening nor contagious ,it is estimated that vitiligo affects between 0.5 and 2% of the world's population with onset being most typical around a person's midtwenties. According to WHO, The prevalence of vitiligo is high in India, varying in the range of 0.46% to 8.8%. The Vitiligo was the most common morphological pattern , other pattern seen are

1. Vitiligo Vulgaris (64.9%)
2. Focal Vitiligo (18.6%)
3. Acrofacial Vitiligo (0.8%)
4. Mucosal Vitiligo (14.8%)
5. Segmental Vitiligo (8.2%)

Vitiligo- Vitiligo is correlated with “Killas” and the imbalance of specific “Doshas” (Vata,Pitta,and Kapha) is believed to play a role in its manifestation.

^Vitiligo(vit-ih-lie-go) is a skin condition that leads to pigmentation issues .Healthy experts believe that it is mainly caused by autoimmune problems. Skin disorder may result in several

discomforts and one should know how to prevent them effectively for leading a trouble- free life , On the other hand the treatment for vitiligo may vary from one patient to another patient that can ultimately help for enhancing the quality of life.[2] **Pathogenesis of Vitiligo-** Vitiligo is a multifactorial polygenic disorder with a complex pathogenesis.It is related to both genetic and non genetic factors.

Although several theories have been proposed about the pathogenesis of vitiligo, the precise cause remains unknown.

The theories include
 Autoimmune and cytotoxicity theory
 Intrinsic defect and melanocytes
 Neural hypothesis
 Oxidant –antioxidant mechanism
 Vitiligo are asymptomatic except in inflammatory vitiligo, which is associated with pruritus and characterized by elevated lesions, and erythematous margins.

(The FOXP3 gene located on the X chromosome was also the risk factor of the Vitiligo)[3]

Causes of Vitiligo-

1. A disorder of immune system
2. Family history
3. Stress severe sunburn
4. Skin trauma
5. Contact with a chemical
6. Lack of pigment (melanin)
7. Environmental triggers
8. Ultraviolet radiation /melanocytes
9. Iron , copper deficiency
10. Chronic inflammatory process

11. Worm invasions

Symptoms-

1. patchy loss of skin color which usually first appears on hands,face and areas around body opening and the genitals .
2. premature whitening or graying of the hair on your scalp,eyelashes,eyebrows and beard
3. loss of the color in the tissue that line the inside the mouth and nose(mucous membrane)
4. changes color in the eye retina

Types of Vitiligo-

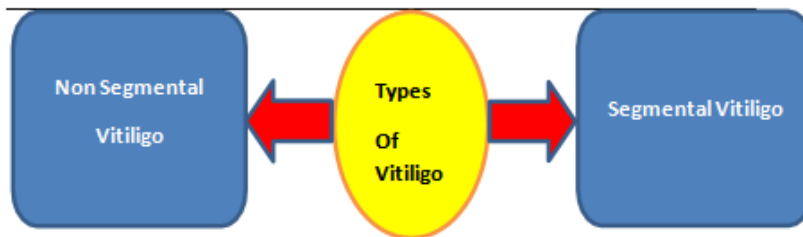


Chart No-2

A)Non-Segmental Vitiligo-Also called bilateral or generalized Vitiligo.In this type the symptoms often appear on both sides of our body as symmetrical white patches. This affects around 9in 10 people with the condition.

Vitiligo.The white patches only affect one area of your body.

Segmental Vitiligo is less common than Non segmental Vitiligo , Although it's more common in children.It's usually starts earlier and affects around 3 to 10 children with vitiligo.

B)Segmental Vitiligo-In segmental Vitiligo also known as Unilateral or Localized

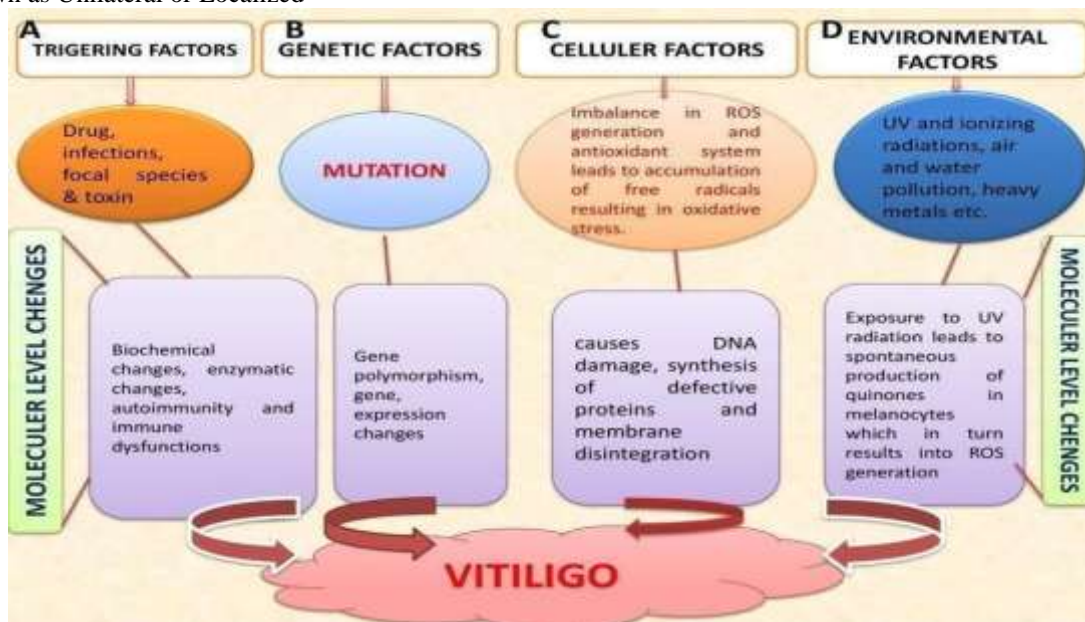
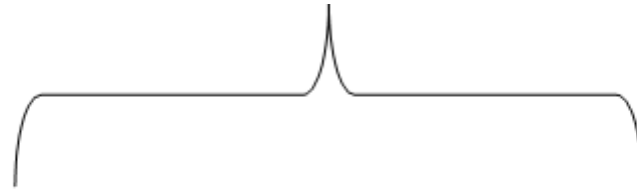


Chart No-3

Therapies used In Vitiligo-The choice of treatment depend on your age how much skin is involved and where how quickly the disease is progressing and how it affecting your life.[5]



A)Light Therapy

A)Light Therapy-phototherapy with narrow band ultraviolet B(UVB)has been shown to stopper slow the progression of active vitiligo.

Frequency of administration – optimal 3 times per week
 Acceptable-2 times per week

Dosing protocol-

1. Initial dose of 200 ml
2. Increase by 10% and 20%per treatment
3. Fixed dosing base on skin prototype is another acceptable dosing strategy that considers the inherent difference in minimal erythema dose(ME3)of various skin types

B)Surgical Therapy

B)Surgical Treatment –

1. Skin grafting
2. Blister grafting
3. Cellular suspension transplant

□**Surgical Grafting** – In this procedure your doctor transfers a very small selection of your healthy pigment skin to areas that have lost pigment.

□**Blister Grafting-** In this procedure your doctor creates blisters on your pigmented skin usually with suction, and then transplants the tops of the blisters to discovered skin.

□**Cellular suspension Transplant**-In this doctor takes some pigmented skin,the cells into a solution and then transplant them onto a prepared affected area.

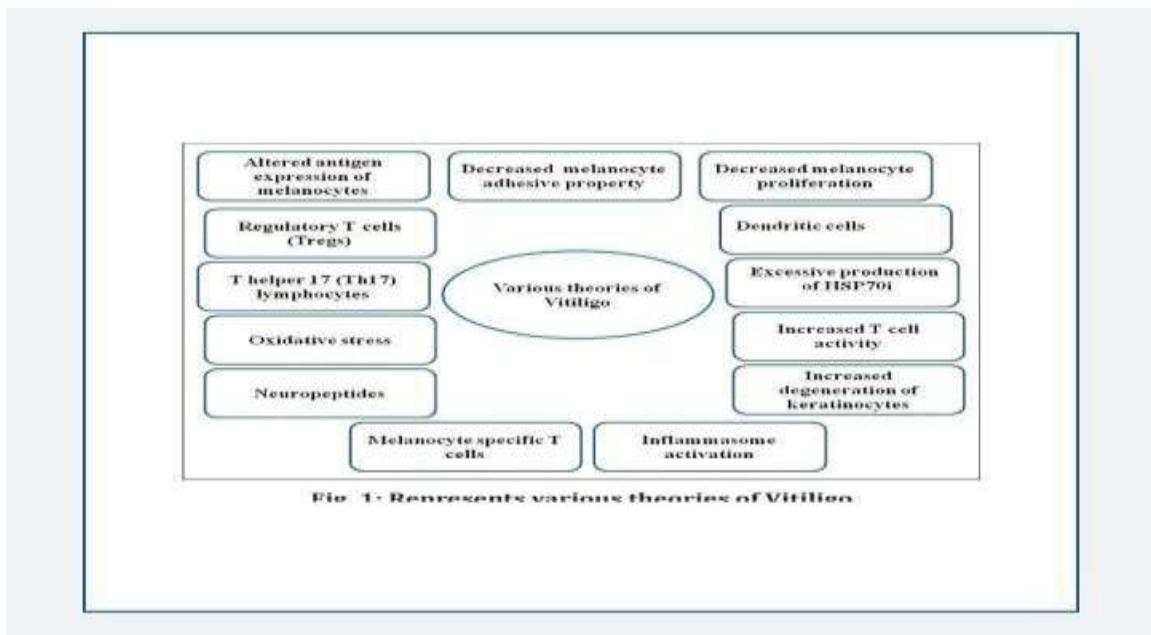


Chart No-4

Animal Models of Vitiligo that develop spontaneously- Several animal species spontaneously develop vitiligo. Sinclair swine depigmentation and cellular and humoral immunity against melanocytes have been reported in association with disease

1) Swine

They were bred to exhibit a high incidence of melanoma -54% of these animals are born with melanoma and 85% of them develop melanoma within the 1st year of life –but in 90% of animals tumor spontaneously resolve and are accompanied by local depigmentation of the skin and hair .Between the 4th week and 16th week of life , depigmentation may then spread from the local sit and generally involve the skin , hair , and melanocytes in the iris of the eye

2)Horses- Little is known about the mechanism of vitiligo in horses containing antibodies against surface melanocyte antigens .42 Therefore ,horses may be helpful models to study antibody formation in vitiligo, particularly because they provide large quantities of serum for antibody purification. Vitiligo due to the gray allele in Lipizzaner horses[7]

Toxicology occur in Vitiligo-

- 1) Acute oral Toxicity
- 2) short term inhalation toxicity
- 3) short term oral toxicity

- 4) chronic oral toxicity
- 5) skin irritation
- 6) cytotoxicity
- 7) Genotoxicity
- 8) Antimutagenicity

Prevention of Vitiligo-

- 1. protect your skin from the sun
- 2. Never use a tanning bed or sun lamp
- 3. Avoid cats, scrapes and burns
- 4. Know the risk of getting the tattoo
- 5. Support your immune system with a healthy style
- 6. Take care of your mental health
- 7. connect with others who have a vitiligo
- 8. drink lots of water or eat healthy food full of good nutrients.

1) Immunotherapy-

Adaptive immunity in Vitiligo –Multiple studies implicate antigen specific CD8+ t cells mediated destruction of melanocytes in human vitiligo. Early observation reported infiltration of T cells in lesional skin from patients with vitiligo, and CD8+ T cells were found adjacent to dying melanocytes in the epidermis.

Further, the frequency of melanocyte antigen treatment positive CD8+ T cells in the blood vitiligo patients correlate with disease severity and these cells are capable of killing melanocytesin-vitro.

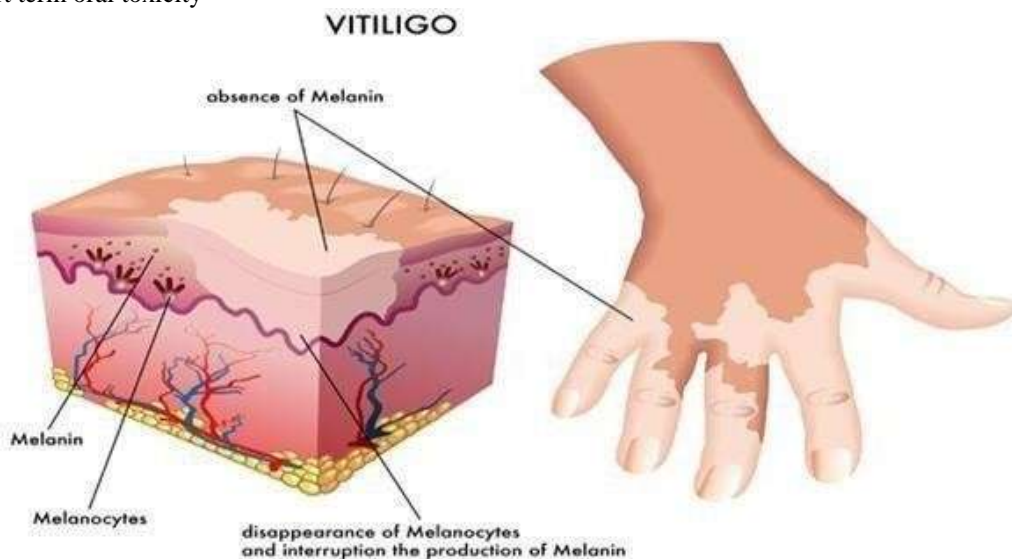


Chart No-5

□**General Mechanism Of vitiligo-** Melanin is produced by skin cells called Melanocytes. (melanocytes gives skin color)
 The foreign invaders like bacteria that can cause harm to your body

Then immune system overreact and develop antibodies to destroy that foreign invaders
 The immune system mistakenly destroyed the melanocytes
 Then white milky patches are form Then cause Vitiligo

□**Synthetic drugs that are used in treatment of Vitiligo-**

Treatment	Drug	Indications	Side effect
1)Corticosteroid	Betamethasone dipropionate,clobetasol dipropionate,	Localized Vitiligo both on adults and children s	Skin atrophy,Telangiect asias, acneic lesions,hypertrichosi s
2)Immunomodulators	Tacrolimus , pimecrolim us	Adult patients as a substitutio n option of corticostero id	Photosensitivity,Bu rning sensation erythema, flushing increased risk of cutaneous.
3)Orally Administered	Ruxolitinib(opzelura)	Medicatio n approved U.v, high risk myelofibro sis	nUrinary tract infection Other bybleeding Increased risk of infection Weight gain

Table N0-1

□**Herbal drug used in the treatment of vitiligo-**

- 1.Capsaicin 2.Walnut
3. Green tea
4. Basil Leaves
5. Giloy

1)	Capsaicin	Curcumas' – melo(muskmelon, fixed 4 to16%)proteins,capsan thin, carotene	They are responsible for red pigment.
2)	walnut	Gallic acid,ethyl gallate, pyrogallol, vanillic acid, protocatechuic acid	They contain copper which is needed to produce melanin pigment.
3)	Green Tea	Caffeine, catechin, epigallocatechin, theanine, epicatechin, gallic acid	Antioxidants Act as booster for
			pigmentation and melanin production.
4)	Basil Leaves	Methyl cinnamate (70.1%) linalool(17.5%)B. elemene	Anti aging Stimulate production of melanin on the skin
5)	Giloy	Giloy, tinospora acetate, Tinosporidine, sinapic acid, octacosanol	A herb that helps treat and correct the abnormalities of one's immune system

Table No-2

- **Capsicum-** Capsicum was first described in the mid-1400 by a physician who accompanied Columbus to the west indies.



Fig 1) -Capsicum

Dose of capsicum- Children-0.025%- 0.075%

Pregnancy- high level of dose avoided

Adults- apply 3 to 4 times a day

Dosage form and Strength[9]

Topical Cream- 0.025%-0.035%, 0.075% to0.1%

Topical gel- 0.025%

Topical liquid- 0.025%

• **Solvent suitable for extraction-**

Solvent and surfactant

1)Ethyl acetate

2)Dichloromethane and Acetone

3)Glycerol

4)Acetonitrile

5)methanol

6)acetic acid

7)toluene

Validation method in Vitiligo-[11]

Validation of UV spectrophotometric method for analysis of capsaicin in Ethanol.

HPLC-Capsaicinmethanol and deionized water (66.34.u/u) by mobile phase.

By UV spectroscopy – Capsaicin Validation carried out by double beam UV visible spectrophotometer by using ethanol as diluent phase, Capsaicin shows maximum absorbance peaks at 227 nm and 280 nm wavelength.

□**Synonym-**

Capsicum extract,Chillies,Cayenne pepper

• **Family - Solanaceae**

• **Biological source-**

Oleoresin of Red-chillies obtained by percolation of dried ripe fruits of capsicums annum van

• **Chemical constituents-**

0.5to0.9% colorless, crystalline and pungent known as capsaicin which volatile above 65 degree celcius , fixed oil (4to16%),protein and pigment. Pigment is responsible for red color .Thiamine and Ascorbic acid

• **Geographical source -**

East Africa, west Africa and India .in India found in Andhra Pradesh ,Uttar Pradesh ,Gujarat ,Maharashtra ,Assam and Tamil Nadu

• **Uses-**

1) Anti-inflammatory and antioxidant

2) Capsaicin used in vitiligo they stop cellular damage

3) Cucumis melo stop deconstruction of melanocytes by oxidative stress in first step of vitiligo

• **MOA-** capsaicin(containing curcumas'-melo,chili pepper,capsanthin,carotene) Act as Antioxidant and Anti-Inflammatory

It blind to the TRPV1 Receptor

Then it stopped cellular damage ROS (role of oxidative stress)

□**Basil leaves-**



Fig 2-Basil Leaves

• **Synonym-**Sweet basil , Basilic commune , Basilic Grand, Krishna Tul

• **Family-** Lamiaceae

• **Chemical constituent-** Methyl cinnamate(70.1%)

Linalool(17.5%) Belemene(2.6%) Camphor (1.5)

• **Geographical sources-**

Tropical Asia, Africa ,America and India

• **Biological sources-**

Basil is obtained from the foliage of ocimum basilicum L.(Sweet basil)

• **Uses-**

1) Basil leaves stimulate the production of melanin

2) It is act as antibacterial and antifungal

3) It used as anti-inflammatory

• **MOA-** Basil leaves , anti aging properties

Mix the leaves with some lime juiceThick paste apply on skin Keep 20 min, then increase the production of melanin.

3) **Walnut-**

• **Synonym-**

Juglandaceae (Latin), English walnut, Black walnut

• **Family- Juglandaceae**



Fig 3-Walnut

- **Chemical constituent-** Ash(3.4%)
 Lignin(50.3%)
 Hemicelluloses(22.4%)
 Cellulose(23.9%)
- **Geographical source-**
 Ancient Persia, USA,China,Turkey
- **Extraction** - Ultrasound
- **Uses-**
 1)Reduction of the white patches caused by vitiligo.
 2)It acts as an antioxidant.
 3)Walnut may decrease inflammation.
- **MOA-** Consume 5-7 walnut daily
 Try making paste by crushing walnut Walnut fine powder mix with some water Apply paste to affected area
 (white patches) Then activate TRPV1
 Receptor in body
 Helpful to reduce patches.
- 3)Gilloy
- **Synonyms-**
 Gulvel ,Tinsopora, Giloy,Amrita
- **Family -Menispermaceae**



Fig 4-Giloy

- **Chemical constituent-**
 Tinsporine ,Tinosporic acid , Tinospora l , Giloin
 ,Berberine , Syringin ,Tinosporidine ,Tinosporaside
- **Biological source-**
 These are the dried leaves and stem pieces of woody climber Tinospora cordifolia,Miers
- **Geographical source-**
- **Uses-**
 1) It is as anti- inflammatory.
 2) It is used as antioxidant
 3) it is act as stimulate the melanin synthesis
- **MOA-** giloy (giloin) Consumed in powdered form , decoction katha Gilloy apply topically too as a paste
 It binds to JAK receptor Which signal mediated melanocyte destruction Giloy helps to minimize effect.
- 4)Tea-
- **Synonym-Camellia thea**
- **Family-Theaceae**



Fig 5-Tea

• **Chemical constituents-**

It is rich source of caffeine (1-3%) .It also contains theobromine and theophylline in minor quantities, gallic acid (15%),yellow volatile oil

• **Geographical source-**

Tea is found in India ,Sri Lanka, China ,Indonesia and Japan.

• **Biological source-**

It contains the prepared leaves and leaf buds of *Thea sinensis*(Linne)O.kuntze .

• **Uses-**

- 1)Green tea is used for improving the skin texture.
- 2) It is used as an antioxidant .
- 3) It acts as anti- anti-inflammatory.

• **MOA-** Green Tea, treating the discomfort of vitiligo

Best home remedy to treat vitiligo.

II. CONCLUSION-

In this Review article we will discuss the use of herbal drugs in Vitiligo, Vitiligo has a complex, Multifactorial pathogenesis .Studies conducted directly in humans and their tissues are important, but are primarily limited to correlated observations. Combining mechanistic studies in animal models with observational studies in humans and their tissues is a powerful approach to better understand vitiligo pathogenesis and develop new treatment for the disease .

Herbal drugs , on the other hand, offer potential alternatives due to their wide range of bioactive compounds and lower risk of adverse effects .However , it is important to note that more research is needed to determine the safety efficacy and optimal dosage of herbal drugs for vitiligo treatment. The lack of standardized formulation and quality control in herbal medicine also poses challenges in their widespread adoption. In summary animal models provide an opportunity for studies to define vitiligo pathogenesis , in this review we will discuss the analysis extraction of herbal compounds by using suitable spectroscopic methods .

REFERENCE -

[1]. Hann SK, Chung HS. Historic view of vitiligo in Korea. *Int J Dermatol* 1977;36:313-315

[2]. Article by Dr.Karanvir Singh(M.D in AYURVEDA,PANCHAKARMA FAGE) and reviewed by Vaidya Jagjit Singh(B.A.M.S)

[3]. Wolff K, Johnson Ra, Suurmond D.Section 13:Pigmentary disorderVITILIGO.In :Fitzpatrick's color atlas and synopsis of clinical Dermatology ,6th ed., editors.New York: McGraw-Hill;2009

[4]. Grimes PE, Miller MM. Vitiligo: Patient stories, self-esteem, and the psychological burden of disease (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986114/>). *Int J Womens Ad*

[5]. American Academy of Dermatology.Vitiligo: An Overview (<https://www.aad.org/public/diseases/a-z/vitiligo-treatment>). Accessed 11/23/2022.

[6]. American Osteopathic College of Dermatology. Vitiligo (<https://www.aocd.org/page/Vitiligo>). Accessed 11/23/2022.

[7]. od Ansan SH, Al. Current remedies for visiting Actimus Rev 2010;9-516-20 Jam P Akhter S. Ancan MZ. Vertigo and its herbal treatment. *Pharm Rev* 2008 12:127-9

[8]. H.E. Teulings, M. Overkamp, E. Ceylan, L. Nieuweboer-Krobotova, J.D. Bos, T. Nijsten, et al. Decreased risk of melanoma and nonmelanoma skin cancer in patients with vitiligo: a survey among 1307 patients and their partners *Br J Dermatol*, 168 (2013), pp. 162-171

[9]. Sampogna F, Raskovic D, Guerra L, et al. Identification of categories at risk for high quality of life impairment in patients with vitiligo. *Br J Dermatol*. 2008 Aug;159(2):351-359

[10]. Govindarajan V., Rajalakshmi D., Chand N., Salzer U.J. Capsicum - production, technology, chemistry, and quality. Part IV. Evaluation of quality. *Crit. Rev. Food Sci. Nutr.* 1987;25:185-282

[11]. 11)Walnut, Agriculture - Transport Information Service". Association for German Insurance. 2010. Archived original on 14 February 2015. from the Parsad D, Pandhi R, Juneja A. Effectiveness of oral Ginkgo biloba in treating limited, slowly spreading vitiligo. *Clin Exp Dermatol*. 2003;28(3):285-7.

- <https://doi.org/10.1046/j.1365-2230.2003.01207.x> PMID: 12780716
- [12]. National formulary of Unani Medicine (2007), Part I, vol 11, Dept of AYUSH, Ministry of Health and family welfare, India Pp; 11-12,31-32,85-86
- [13]. Mehta N, Shah KC, Theodore C et al. Epidemiologic Study of Vitiligo in Surat area, south Gujarat Indian J Med Res. 2018; 61:145-154.
- [14]. 36. Arora, A.K.; Kumaran, M.S. Pathogenesis of vitiligo: An update. *Pigment Int.* 2017, 4, 65.3
- [15]. 73. Singh, H.; Kumaran, M.S.; Bains, A.; Parsad, D. A randomized comparative study of oral corticosteroid mini pulse and low-dose oral methotrexate in the treatment of unstable vitiligo. *Dermatology* 2015, 231, 286–290. [CrossRef]74.
- [16]. Ezzedine K, et al Revised classification/nomenclature of vitiligo and related issues: the Vitiligo Global Issues Consensus Conference. *Pigment cell & melanoma research*, 2012 May 1; 25(3):5. Ferzli GM et al., Painting a More Colorful Picture: A Review of Recently Proposed Vitiligo Treatments. *Pigmentary Disorders*, 2014; 1: 143.6. Roy AK et al., Vitiligo: A White Patch that Affects the Soul. *Pigmentary Disorders*, 2017,4: 254.
- [17]. Roy AK et al., Vitiligo: A White Patch that Affects the Soul. *Pigmentary Disorders*, 2017,4: 254. 2) REGHU et al., Epidemiological profile and treatment pattern of vitiligo in a tertiary care teaching hospital, 2011; 2: 2-5. 3) Dell'Anna ML et al., A review and a new hypothesis for non-immunological pathogenetic mechanisms in vitiligo. *Pigment Cell & Melanoma Research*, 2006 Oct 1; 19(5): 406-11.
- [18]. F.S. Hodi, S.J. O'Day, D.F. McDermott, R.W. Weber, J.A. Sosman, J.B. Haanen, et al. Improved survival with ipilimumab in patients with metastatic melanoma *N Engl J Med*, 363 (2010), pp. 711-723
- [19]. N.C. Laddha, M. Dwivedi, M.S. Mansuri, A.R. Gani, M. Ansarullah, A.V. Ramachandran, et al.
- [20]. Vitiligo: interplay between oxidative stress and immune system *Exp Dermatol*, 22 (2013), pp. 245-250
- [21]. *Capsicum annuum* L. USDA, NRCS. 2007. The PLANTS Database (<http://plants.usda.gov>, May, 2009). National Plant Data Center, Baton Rouge, LA 70874-4490 USA.
- [22]. Leung AY. *Encyclopedia of Common Natural Ingredients Used in Food, Drugs and Cosmetics*. New York, NY: Wiley; 1980.
- [23]. Buck SH, Burks. Capsaicin: hot new pharmacological tool. *Tips*. 1983;4:84-87.
- [24]. Yewale S., Farash Z., Kulkarni S., Palghadmal S., Athawale N., Sawant L., Bhope S., Padmanabhan S. Effect of solvent polarity on extraction yield of total flavonoids with special emphasis to glabridin from *Glycyrrhiza glabra* roots. *Fab J. Pharm. Sci.* 2022;1:1–12.
- [25]. Bley K., Boorman G., Mohammad B., McKenzie D., Babbar S. A comprehensive review of the carcinogenic and anticarcinogenic potential of capsaicin. *Toxicol. Pathol.* 2012;40:847–873. [PubMed] [Google Scholar]
- [26]. Srinivasan K. Biological activities of red pepper (*Capsicum annuum*) and its pungent principle capsaicin: a review. *Crit. Rev. Food Sci. Nutr.* 2016;56:1488–1500.
- [27]. Govindarajan V., Rajalakshmi D., Chand N., Salzer U.J. Capsicum - production, technology, chemistry, and quality. Part IV. Evaluation of quality. *Crit. Rev. Food Sci. Nutr.* 1987;25:185–282.
- [28]. Barbero G.F., Liazid A., Palma M., Barroso C. Ultrasound-assisted extraction of capsaicinoids from peppers. *Talanta*. 2008;75:1332–1337. doi: 10.1016/j.talanta.2008.01.046. [PubMed] [CrossRef] [Google Scholar].
- [29]. Laskaridou-Monnerville A. Determination of capsaicin and dihydrocapsaicin by micellar electrokinetic capillary chromatography and its application to various species of *Capsicum solanaceae*. *J. Chromatogr. A.* 1999;838:293–302. doi: 10.1016/S0021-9673(98)00969-8.
- [30]. Dr .C.K Kokate M Pharm ,ph D, F.U.G.E.E.S (Germany)Vice chancellor,KLE University JNMC Campus ,Nehru Nagar , Belgaum 590010, India